10c. Preparative GLC of a portion of the more volatile distillate [bp 82–88 °C (5 mm)] gave a sample of **10c**: ^{1}H NMR (CCl_4) δ 4.10 (2 H, q, J = 7 Hz), 3.10 (6 H, s), 2.38 (3 H, br s), 2.27 (2 H, br s), 1.23 (3 H, t, J = 7 Hz).

3-Oxocyclobutanecarboxylic Acid (1a). Diisopropyl 3,3-dimethoxycyclobutane-1,1-dicarboxylate (**7d**) (287.5 g, 1.0 mol) was stirred with 20% hydrochloric acid (750 mL) at reflux for 60 h.

After cooling, the solution was continuously extracted with ether for 18 h. The ether was removed at reduced pressure, leaving a yellow oil, which crystallized on standing and proved to be the title acid (111 g, 97%), which was characterized by conversion to its ethyl ester, whose physical properties were in accord with literature data:[15] ^{1}H NMR (CCl_4) δ 4.17 (2 H, q, J = 7 Hz), 3.27 (5 H, m), 1.27 (3 H, t, J = 7 Hz); ^{13}C NMR (CCl_4) 201.48 (C_3), 173.21 (CO_2), 60.57 (OCH_2), 51.20 ($C_{2,4}$), 27.09 (C_1), 14.09 (CH_3).

Acknowledgment. We thank the Flinders University of South Australia for financial support, the National Research Fellowships Advisory Committee for a Queen Elizabeth II Award (to P.E.P.), and Dr. E. W. Della for valuable discussions.

Registry No. **1a**, 23761-23-1; **6**, 22094-18-4; **7c**, 115118-67-7; **7d**, 115118-68-8; **10c**, 115118-69-9; $CH_2(CO_2Et)_2$, 105-53-3; $CH_2(CO_2Pr\text{-}i)_2$, 13195-64-7; $EtCH(CO_2Et)_2$, 133-13-1.

A Highly Versatile Synthesis of 2,2-Dimethyl-3-(2,2-dichlorovinyl)cyclopropane-1-carboxylic Acid Esters

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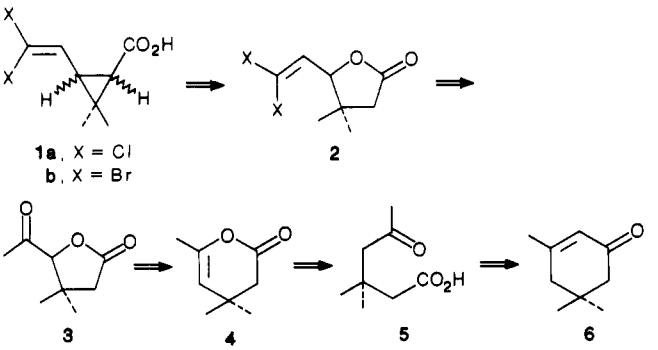
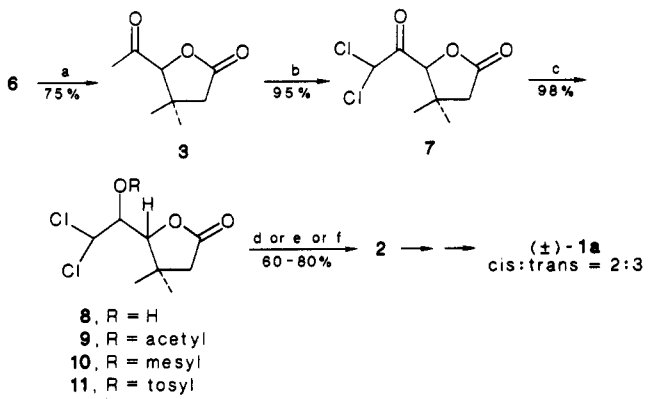
The esters of 2,2-dimethyl-3-(2,2-dihalovinyl)cyclopropane-1-carboxylic acids, which are structurally similar to naturally occurring chrysanthemates, have emerged as one of the most important classes of agricultural insecticides in recent years.[1] These compounds, known as pyrethroids, possess extraordinarily high insecticidal activity, low mammalian toxicity, biodegradability, and considerable increased photostability compared to the natural chrysanthemates.[2] Consequently, much research and development activity were put forward to develop elegant and cost-effective routes to the most potent precursor, 2,2-dimethyl-3-(2,2-dihalovinyl)cyclopropane-1-carboxylic acid (**1**).[3] As part of a general program to develop newer synthetic methodologies to **1** based on readily available and inexpensive raw materials, we reported recently two independent approaches for the syntheses of (1*R*)-*cis*-(+) acids **1a** and **1b** from (+)-3-carene.[4] Further to this work we report herein a short synthesis of *cis*/*trans*-(±)-**1a**, an important precursor for commercial permethrin and cypermethrin, from a readily available and inexpensive raw material, isophorone (**6**).[5]

Scheme I



Scheme II[a]



[a] Reagents: (a) 3.5 mol of $KMnO_4$, 30% aqueous AcOH; (b) SO_2Cl_2, *p*-TsOH·$2H_2O$ (cat.), 60 °C, 2 h or Cl_2, *N*-formylpyrrolidine hydrochloride (cat.), 25 °C, 3 h; (c) 0.3 mol of $NaBH_4$, MeOH, 25 °C, 1 h; (d) *p*-TsCl, 20% aqueous NaOH, 80 °C, 2 h; (e) $SOCl_2$, pyridine, 80 °C, 24 h; (f) DBU, 100 °C, 3 h.

In formulating our synthetic strategy to *cis*/*trans*-(±)-**1**, we viewed the retrosynthetic pathway (Scheme I) with particular attention. It occurred to us that isophorone (**6**) possesses a molecular geometry that is tailor-made for the synthesis of the key intermediate **2**[6] via the lactone **3**. The synthesis of **3** could be conceivable from the enol lactone **4** by the recently reported bromolactonization technique.[7] The enol lactone **4** in turn could be obtained from isophorone (**6**) via its oxidation product **5**.

The synthesis is outlined in Scheme II. With a view to obtain enol lactone precursor **5**, the oxidation of isophorone (**6**) was attempted with potassium permanganate. Thus, when the oxidation was carried out in aqueous acetic acid, to our surprise, lactone **3** was directly obtained as the major product in addition to keto acid **5**. The best yield of **3** was, however, obtained when the oxidation was carried out in 30% aqueous acetic acid. Purification by simple acid–base extraction followed by distillation furnished **3** and **5** in 75% and 10% yields, respectively. Thus, it was possible to achieve three different reaction sequences (Scheme I) in just one pot!

Conversion of **3** to the corresponding dichloro derivative **7** proceeded in near-quantitative yield, either with sulfuryl chloride or with chlorine in the presence of a catalyst.

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(2) Elliot, M. *ACS Symp. Ser.* **1977**, *No. 42*, 1. (b) Elliot, M. *Pestic. Sci.* **1980**, *11*, 119.

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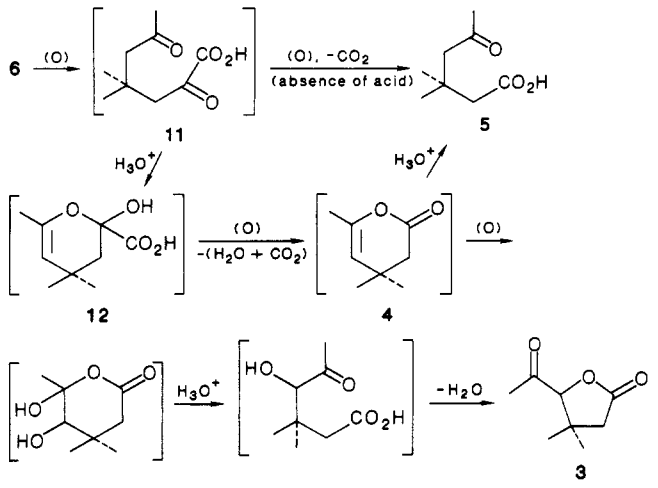
Scheme III



Reduction of 8 with sodium borohydride furnished alcohol 8, as a mixture of diastereomers (9:1),[8] in 98% yield. The acid-catalyzed dehydration of this alcohol mixture to olefin 2 was unsuccessful even with stronger acids, e.g., methanesulfonic acids and trifluoromethanesulfonic acid. In all cases, the starting material was recovered in excellent yield. The dehydration of 8 to 2, however, could be effected in 50% yield with thionyl chloride and pyridine. Alternatively, mesylate 10 (8, 1.1 MsCl, pyridine, 25 °C, 4 h) or tosylate 11 (8, 1.1 TsCl, pyridine, 0 °C, 24 h) on heating with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) furnished 2 in 75% yield. More conveniently, the dehydration of 8 was carried out at 25 °C by using a combination of *p*-toluenesulfonyl chloride and aqueous sodium hydroxide[9] to yield 2 in 80% yield. As stated earlier, there exist a large number of patents on the conversion of 2 to the desired *cis/trans*-(±)-**1a** (2:3).[6] This, therefore, completes our formal synthesis of *cis/trans*-(±)-**1a** from isophorone (6).

The oxidation of isophorone (6) with potassium permanganate needs special mention in order to comment on the mechanism of this transformation. It was observed that the formation of the relative amounts of 3 and 5 is dependent on the pH of the reaction medium. Thus, while the oxidation in 40%, 30%, and 15% aqueous acid concentration, yielded 86:14, 85:15, and 80:20 of 3 and 5, respectively, the corresponding reaction in water (pH of the oxidation medium becomes alkaline) yielded 5 as the sole product. The possible intermediacy of pyranone 4[10] toward the formation of 3 was established by its reaction with potassium permanganate in 30% aqueous acetic acid, which yielded lactone 3 together with some 2,2-dimethylsuccinic acid. However, that 4 was not formed from keto acid 5 (Scheme I) under the reaction conditions was evident from the observation that 5 on prolonged treatment with potassium permanganate under the above conditions did not produce 3; instead the starting material was recovered unchanged. An alternate mechanism is therefore proposed to explain the formation of 3 and 5 from 6 via intermediate 4 (Scheme III).

Oxidation of 6 with $KMnO_4$ would produce intermediate 11, which would undergo further oxidation to 5 in the alkaline medium. In the acidic medium, 11 would undergo acid-catalyzed cyclization to 12, which after oxidative decarboxylation would furnish 4. Hydroxylation of 4 with aqueous $KMnO_4$ followed by lactonization as shown would yield lactone 3. Our attempts to isolate 11 to substantiate the above mechanism further were unsuccessful.

Experimental Section

Melting points and boiling points were uncorrected. NMR spectra were recorded in $CDCl_3$ on Bruker CW-80 and Bruker AC-80 spectrometers, with chemical shift reported in ppm downfield of internal standard tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. GLC analyses were carried out on a HP 5890 gas chromatograph using capillary column HP 101 (methylsilicone) (25 m × 0.2 mm × 0.2 μm film thickness). GC–MS analyses were carried out on a Hewlett-Packard 5993 B spectrometer using 2% OV-210 on Chromosorb WHP 80/100 (2 m × 0.6 cm column). All starting materials were reagent grade, were obtained from commercial suppliers, and were used without purification.

5-Acetyldihydro-4,4-dimethyl-2(3*H*)-furanone (3). To a solution of isophorone (27.6 g, 0.20 mol) in acetic acid (250 mL) and water (580 mL) maintained at ice water bath temperature was added portionwise powdered potassium permanganate (111 g, 0.70 mol). The reaction mixture was stirred for 0.5 h at 25 °C and then cooled to 0–5 °C. Sulfur dioxide gas was passed through the reaction mixture till the reaction mixture became clear. The supernatant liquid was filtered from the precipitated manganous sulfate and extracted with chloroform (3 × 50 mL). The solid was washed with chloroform (50 mL), and the washing was added to the organic layer that was evaporated. The residue obtained was digested with aqueous sodium bicarbonate solution and extracted with chloroform (100 mL). Evaporation of the chloroform layer yielded pure 3 (23 g, 75%), which was distilled under vacuum: bp 80–85 °C/1 mmHg; 99% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 1795, 1720; ^1H NMR (80 MHz) δ 4.45 (s, 1 H, CHO), 2.45 (s, 2 H, CH_2CO), 2.27 (s, 3 H, $CH_3C{=}O$), 1.35 (s, 3 H, CH_2), 1.05 (s, 3 H, CH_3); GC–MS (70 eV) M^+ 156 (20), 113 (94), 95 (25), 85 (35), 57 (40), 43 (100), 41 (50), 29 (35). Anal. Calcd for $C_8H_{12}O_3$: C, 61.54; H, 7.69. Found: C, 61.34; H, 7.60.

The aqueous layer was acidified with concentrated HCl and then extracted with chloroform (50 mL). Evaporation of the chloroform layer followed by distillation yielded 5 (3.1 g, 10%): bp 101–106 °C/1 mmHg; 97.5% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 3600–3100 (b), 1720, 1700; ^1H NMR (80 MHz) δ 8.0–7.4 (s, 1 H, OH), 2.6 (s, 2 H, CH_2CO), 2.48 (s, 2 H, CH_2CO_2), 2.13 (s, 3 H, $CH_3C{=}O$), 1.13 (s, 6 H, 2 CH_3).

5-(Dichloroacetyl)dihydro-4,4-dimethyl-2(3*H*)-furanone (7). A mixture of 3 (15.6 g, 0.1 mol), sulfuryl chloride (54 g, 0.4 mol), and *p*-toluenesulfonic acid dihydrate (1.04 g, 0.005 mol) was stirred at 60 °C for 2 h. Excess sulfuryl chloride was distilled off and water (40 mL) was added. The reaction mixture was extracted with dichloromethane (3 × 40 mL). The organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off. Distillation under vacuum furnished 7 (21.4 g, 95%; bp 92–94 °C/0.5 mmHg), which solidified on standing: mp 55–56 °C; 99.5% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 1800, 1750; ^1H NMR (80 MHz) δ 6.25 (s, 1 H, $CHCl_2$), 4.92 (s, 1 H, CHO), 2.55 (d, 2 H, J = 1 Hz, CH_2), 1.48 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3). Anal. Calcd for $C_8H_{10}O_3Cl_2$: C, 42.67; H, 4.44. Found: C, 42.43; H, 4.45.

5-(1-Hydroxy-2,2-dichloroethyl)dihydro-4,4-dimethyl-2-(3*H*)-furanone (8). To a solution of 7 (22.5 g, 0.1 mol) in methanol (100 mL) was added portionwise sodium borohydride (1.06 g, 0.028 mol) at 25 °C. The reaction mixture was stirred for 1 h at 25 °C, acidified with 10% aqueous HCl solution, and extracted with dichloromethane (3 × 50 mL). The organic layer was dried and the solvent was distilled off to yield 8 (22.5 g, 98%) as mixture of diastereoisomers (9:1),[8] which solidified on standing: mp 68–69 °C; 99% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 3650–3100, 1790, 1750; ^1H NMR (500 MHz) δ 6.11 (s, 1 H, $CHCl_2$), 4.07 (s, 1 H, J = 9.5 Hz, $OCHCHCl_2$), 4.04 (dd, 1 H, J = 9.5 Hz, J = 5.1 Hz, CHO), 2.75 (d, 1 H, J = 5.2 Hz, OH), 2.50 (d, 1 H, J = 17 Hz, HCH), 2.35 (d, 1 H, J = 17 Hz, HCH), 1.35 (s, 3 H, CH_3), 1.2 (s,

(8) Analyzed as acetate 9 (mp 115–116 °C) by GC–MS using capillary column HP 101 (methylsilicone fluid) (25 m × 0.2 mm × 0.2 μm film thickness, column temperature 180 °C, injection port and detection temperature 250 °C, flow split ratio 50:1, capillary 1 mL): retention time 5.75 and 6.32 min; MS (70 eV, CI) m^+ m/e 268 for both components.

(9) (a) Lee Graham, R. U.S. Pat. 4 289 711, Burroughs Wellcome, 1982. (b) Jpn. Pat. 76/145168 (1975) and 76/146442 (1975), Kuraray Co. Ltd.

(10) Prepared by following the literature procedure: Lehky, P.; Kronig, P. Eur. Pat. Appl. EP65708; *Chem. Abstr.* **1983**, *98*, P106865Z. We thank a referee for bringing this to our attention.

3 H, CH_3); GC–MS (70 eV) M^+ 227 (1), 149 (10), 143 (8), 113 (100), 95 (11), 85 (32), 83 (25), 56 (63), 55 (30), 43 (68), 41 (70), 39 (33), 29 (45). Anal. Calcd for $C_8H_{12}O_3Cl_2$: C, 42.29; H, 5.29. Found: C, 41.99; H, 5.36.

5-(2,2-Dichloroethenyl)dihydro-4,4-dimethyl-2(3*H*)-furanone (2). A mixture of **8** (6.81 g, 0.03 g, 0.03 mol), *p*-toluenesulfonyl chloride (8.33 g, 0.035 mol), and 20% aqueous sodium hydroxide solution (18 mL, 0.09 mol) was stirred at 25 °C for 3 h. The reaction mixture was extracted with chloroform (3 × 30 mL), and the organic layer was dried over anhydrous sodium sulfate. Removal of solvent yielded **2** (5.01 g, 80%), which was distilled under vacuum to yield pure **2** as a pale yellow oil: bp 100–101 °C/0.5 mmHg; 97% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 1795 1740 (s), 1630; ^1H NMR (80 MHz) δ 5.94 (d, 1 H, J = 11 Hz, CH=), 4.88 (d, 1 H, J = 11 Hz, CHO), 2.4 (d, 2 H, J = 1 Hz, CH_2), 1.23 (s, 3 H, CH_3), 1.1 (s, 3 H, CH_3).

Reaction of Pyranone 4 with $KMnO_4$ in 30% Aqueous Acetic Acid. Pyranone **4** was prepared from keto acid **5** by acid-catalyzed dehydration in refluxing toluene with simultaneous removal of water azeotropically.[10] The product was distilled to yield pure **4**: bp 38–40 °C/0.6 mmHg; 99% (GC); IR ($CHCl_3$) (ν, cm^{-1}) 1770, 1700; ^1H NMR δ 4.87 (s, 1 H, CH=), 2.40 (s, 2 H, CH_2), 1.86 (d, 3 H, J = 1.3 Hz, CH_3), 1.08 (s, 6 H, 2 CH_3).

To a solution of pyranone **4** (420 mg, 3 mmol) in 30% aqueous acetic acid (4.0 mL) cooled in an ice water bath was added $KMnO_4$ (237 mg, 1.5 mmol). The usual workup provided a neutral fraction (320 mg) containing 65% **4** and 35% **3** (as analyzed by NMR or GC) and an acidic fraction (80 mg) containing keto acid **5** (15%) (by NMR) and 2,2-dimethylsuccinic acid, mp 138–140 °C (lit.[11] mp 141 °C).

Acknowledgment. We thank IEL Limited for support and the Tata Institute of Fundamental Research, Bombay, for 500-MHz NMR facilities.

Registry No. *trans*-(±)-**1a**, 55701-07-0; *cis*-(±)-**1a**, 55701-06-9; **2**, 115118-27-9; **3**, 115118-28-0; **4**, 68208-62-8; **5**, 20624-63-9; **6**, 78-59-1; **7**, 115118-29-1; **8** (diastereomer 1), 115118-30-4; **8** (diastereomer 2), 115118-31-5.

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An Efficient, Palladium-Catalyzed Route to Protected Allylic Amines

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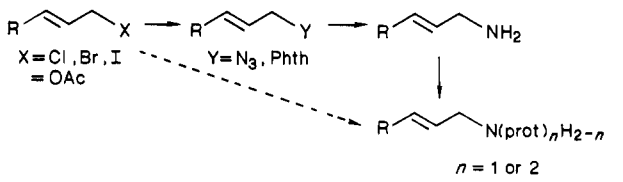
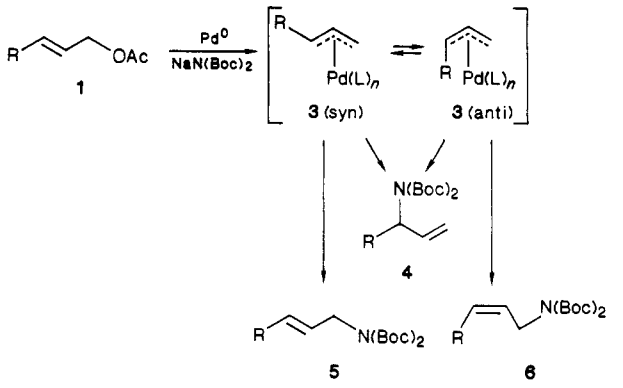
Because of their occurrence in a number of natural products, the development of methodology directed toward the synthesis of primary allylic amines is an active area of research in organic chemistry.[3,4] Among the methods that have been developed is the palladium-catalyzed conversion of allylic acetates and chlorides to the corresponding amines. Phthalimide,[5] sodium azide,[6] *p*-toluenesulfonamide,[7] and 4,4′-dimethoxybenzhydrylamine[8] have been shown to be useful nucleophiles in these reactions. Although the intermediates formed from these reactions can then be converted to the amine, the conditions for this transformation are often quite harsh. For example, phthalimides are often removed by hydrazine in refluxing ethanol, while the substituted benzhydrylamine group is subjected to hot formic acid to effect cleavage.

Scheme I

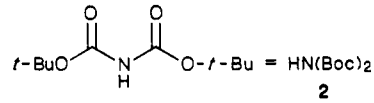


Scheme II



As part of our ongoing interest in the synthesis of various antibiotics, we sought to develop a direct method for the conversion of allylic acetates into suitably protected primary amines. Such an approach would avoid the multistep sequences involved with substitution reactions of azide and phthalimide (Scheme I).

To this end, we began to study acetamide and *t*-butyl carbamate as nucleophiles. Their reactions would supposedly lead directly to N-acyl- and *N*-Boc-protected primary amines.[9] Unfortunately, these compounds were unreactive as nucleophiles in both their neutral and metalated forms.[10] Based on the successful use of malonates and other stabilized nucleophiles in palladium-catalyzed reactions,[11] we then looked at di-*tert*-butyl iminodicarbonate (**2**) as a nucleophile.



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(1) University of Notre Dame.
(2) Royal Institute of Technology.
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